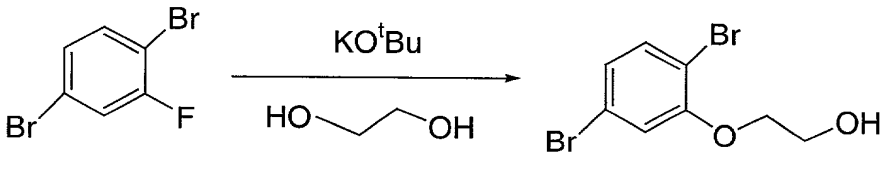
In Reaction Scheme G, deprotection of the compound (19) by removing protecting groups with concentrated HCl in acetonitrile at a temperature about 0°C to about 25°C followed by crystallization of its benzylamine salt affords the penultimate intermediate (20) in quite high yield and purity. When alkyl substituent is isopropyl in compound (19), deprotection occurs after treating the reaction mixture with MsOH, MeOH and then NaOH (aq) at a temperature about 40°C. Salt breaking in citric acid followed by hydrogenation of the benzylamine salt (20) over palladium under hydrogen (about 40 psi) in a protic solvent at a temperature range of about 25°C to about 40°C affords the desired product of carboxylic acid (21) in high yield. The protic solvent is selected from methanol, ethanol, isopropyl alcohol (IPAc), methanol/THF and methanol/DMF. Methanol is a preferred solvent. Addition of THF or DMF may be necessary to remove the catalyst after the hydrogenation. Work up of the reaction mixture followed by crystallization in methanol, THF/water or DMF/water affords the desired compound (21) in high yield (90-95% yield).

The following examples illustrate the preparation of the compound of Formula I and as such are not to be considered as limiting the invention set forth in the claims appended hereto.

EXAMPLE 1

1,4-Dibromo-2-hydroxyethoxybenzene (2)



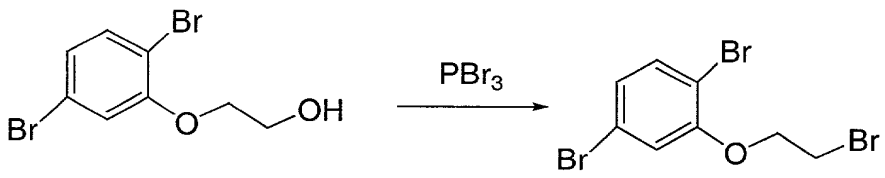
1 **2**

Under nitrogen, to a three-necked flask is added ethylene glycol (350mL), 1,4-dibromo-2-fluorobenzene, **1** (68.6g, 270mmol) and 1-methyl-2-pyrrolidinone (35mL). Solid potassium *tert*-butoxide (112g, 950mmol) is added over 5 minutes. The batch is heated to 97°C to 100°C and aged at the same temperature for 8 hours until HPLC indicated <1.0% of starting material. The batch is then

allowed to cool to about 24°C, and water (137mL, 2mL/g **1**) is added over 0.5 hour. The mixture is filtered, and the solid is washed with ethylene glycol. About 1.2L of water is added to the combined filtrate, which is wash for over 30 minutes. The mixture is then cooled to about 15°C and aged for about an hour. The solid is collected by filtration, washed with water, and dried by suction under nitrogen. Alcohol product **2** is isolated as a light yellow solid (69.6g, 87% yield, 100 A% pure). HPLC conditions: Zorbax RX-C18, 4.6 x 250; MeCN/0.1% H_3PO_4; 1.5mL/min; UV detector at 220nm; Retention times (min): 1,4-dibromo-2-fluorobenzene **1** (9.6), 1,4-dibromo-2-hydroxyethoxybenzene **2** (5.4) and dimer **5** (13.8).

EXAMPLE 2

2-Bromoethoxy-1,4-dibromobenzene (3)



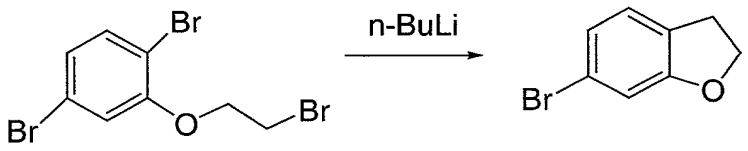
2 **3**

To a solution of 1,4-dibromo-2-hydroxyethoxybenzene (10.05g, 33.9mmol) in toluene (72mL) is added PBr_3 (1.45mL, 15.27mmol). The mixture is heated to about 90°C and aged for about two hours. The remainder of the PBr_3 is added followed by water. The batch is heated at about 90°C for an additional 8 hours and then cooled to room temperature. The batch is slowly quenched with 60mL of 1N NaOH for about 30 minutes. The two layers are separated. The organic layer is washed with water and saved for the next step.

HPLC conditions: Zorbax RX-C18, 4.6 x 150; MeCN/0.1% H_3PO_4 at 1.0 mL/min; UV detector at 230nm; Retention times (min): 2-bromoethoxy-1,4-dibromobenzene **3** (10.5 min)

EXAMPLE 3

6-Bromo-2,3-dihydrobenzofuran (4)



3 **4**

The tribromide solution from the previous step is concentrated to about 10L and flushed with 20L of dry toluene. The final volume is about 8L before the addition of 18L of THF. The batch is cooled to about -73°C and n-butyllithium (1.6M in hexane, 6.0L) is added slowly, keeping the temperature < -70°C. The starting material is assayed by HPLC for 15 minutes after the completion of the addition, and then more *n*-butyllithium is added (a total of 0.4L) until no starting material is detected by HPLC. Excess n-butyllithium is quenched with acetic acid before the batch is allowed to warm to 0°C. About 17L of water is added and the two layers are separated. The organic layer is washed with 0.5N NaOH and water. The batch is concentrated to about 8L and flushed with methanol. The final volume is adjusted to about 8L and the batch is cooled to about 15°C to about 20°C until some product crystallized, whereupon about 7L of water is added over two hours (final methanol:water is about 1:1). The batch is aged at about 15°C for about an hour and then filtered. The solid is washed with 2:3 methanol:water and dried by suction under nitrogen for about six hours. Product **4** is isolated as a white solid (1.71 kg, KF = 7.3µg/1g, 95.07A%, 97wt%, and 85.5% corrected yield).

HPLC conditions: Zorbax SB-C8 4.6 x 250; MeCN/0.1% H_3PO_4 at 1.5mL/min; UV detector at 220nm; Retention times (min): 6-bromo-2,3-dihydrobenzofuran **4** (7.4).